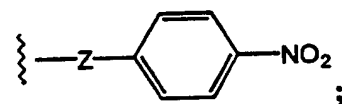
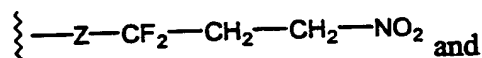
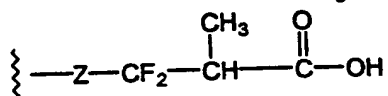
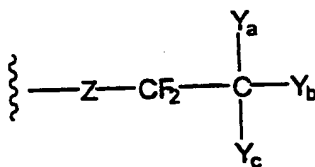
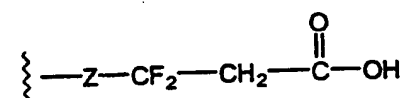
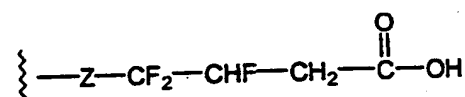
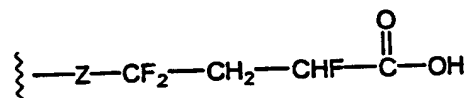
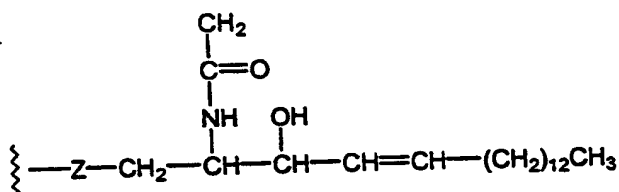
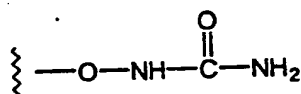
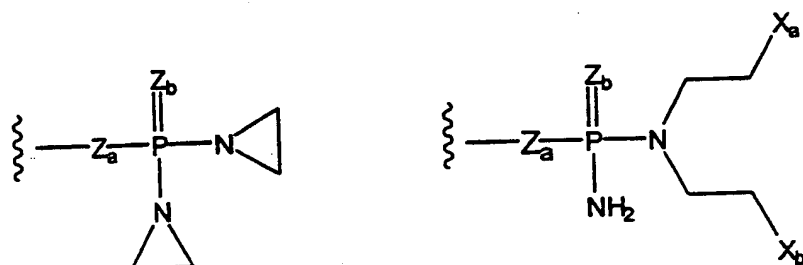


$\text{CH}=\text{C}(\text{R}^{15})_2$  or a substituent having the structure:



10

wherein  $\text{X}_a$  and  $\text{X}_b$  are independently the same or different and are selected from the group consisting of Cl, Br, I, and a potent leaving group;

wherein  $Y_a$ ,  $Y_b$  or  $Y_c$  are independently the same or different and are H or F;

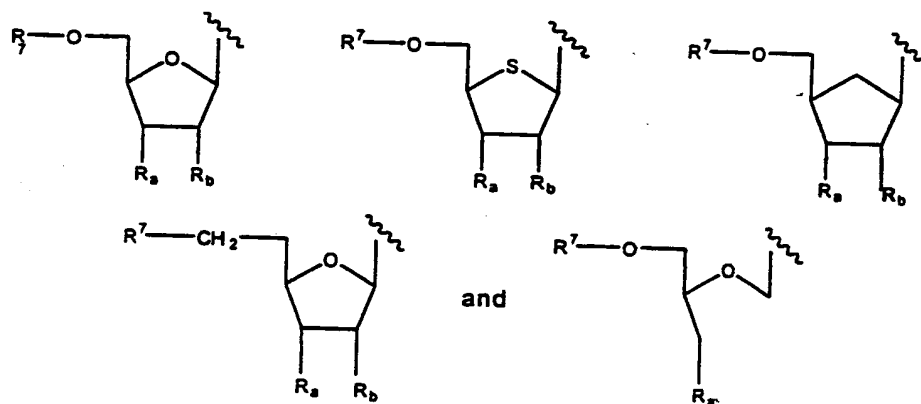
wherein Z,  $Z_a$  and  $Z_b$  are independently the same or different and are selected from the group consisting of O and S; and

5 wherein  $R^{14}$  is H or F, providing if  $R^{14}$  is F, then a is 1 and  $R^{12}$  and  $R^{13}$  are both oxo; and

wherein Q is selected from the group consisting of a sugar, a carbocyclic, and an acyclic compound, or a masked phosphate derivative or phosphoramidate derivative thereof.

10

2. The compound of claim 1, wherein Q is selected from the group of substituents having the structure:

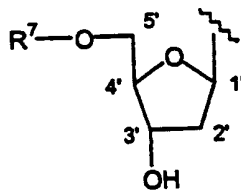


15 wherein  $R_a$  and  $R_b$  are independently the same or different and are selected from the group consisting of Br, Cl, F, I, H, OH,  $OC(=O)CH_3$ , and a protected hydroxyl group; and

wherein  $R^7$  is attached to Q at the 5' position of Q and is selected from the group consisting of a hydrogen, a phosphate group, a phosphodiester group or a phosphoramidate group;

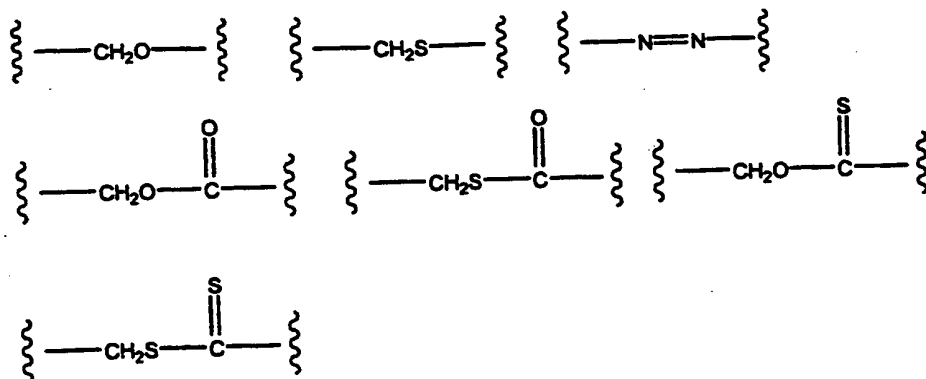
20 and wherein the compound may be in any enantiomeric, diastereomeric, or stereoisomeric form, including D-form, L-form,  $\alpha$ -anomeric form, and  $\beta$ -anomeric form.

3. The compound of claim 2, wherein Q is:

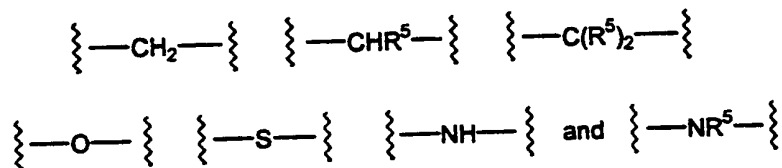
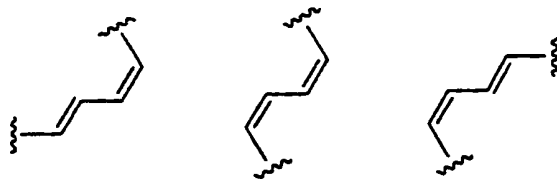


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4. The compound of claim 1, wherein m is 0 and  $R^2$  is selected from the group consisting of:



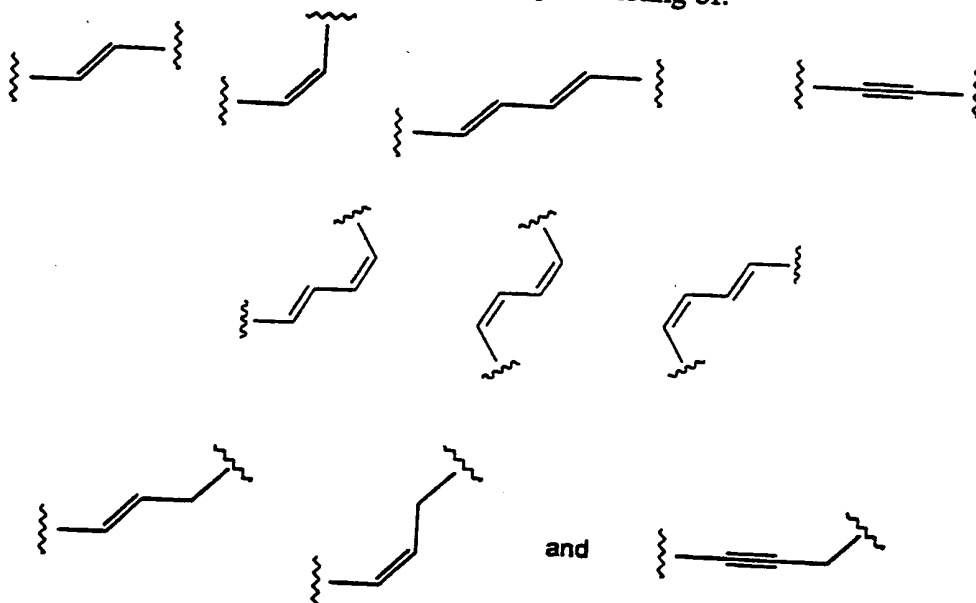
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wherein  $R^5$  is independently the same or different and is selected from the group consisting of a linear or branched alkyl group having from 1 to 10 carbon atoms, a cycloalkyl group having from 3 to 10 carbon atoms, CN and a halogen.

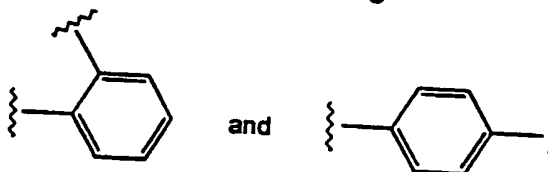
15

5. A compound of claim 1, wherein  $R^2$  and  $R^3$  taken together is an alkenyl or alkynyl and is selected from the group consisting of:



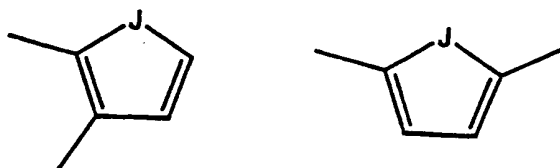
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6. A compound of claim 1, wherein  $m$  is 0 and  $R^2$  is an aromatic hydrocarbyl group selected from the group consisting of:



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7. A compound of claim 1, wherein  $m$  is 0 and  $R^2$  is a heteroaromatic group selected from the group consisting of:

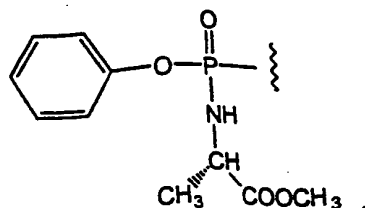


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wherein  $J$  is selected from the group consisting of  $-O-$ ,  $-S-$ ,  $-Se-$ ,  $-NH-$ , and  $-NR^{ALK}-$ .

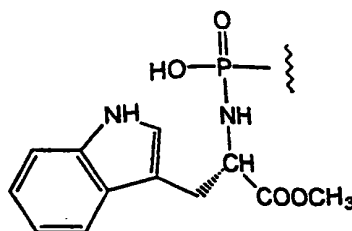
and wherein  $R^{ALK}$  is a linear or branched alkyl having 1 to 10 carbon atoms or a cycloalkyl group having 3 to 10 carbon atoms.

8. A compound of claim 2, wherein  $R^7$  is:



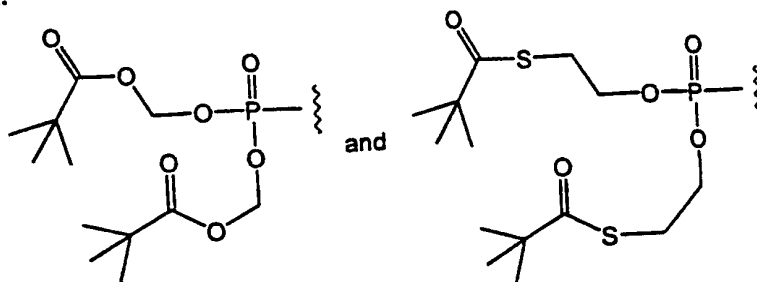
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9. A compound of claim 2, wherein  $R^7$  is:

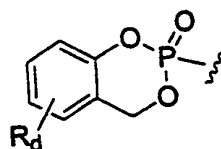


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10. A compound of claim 2, wherein  $R^7$  is selected from the group consisting of:

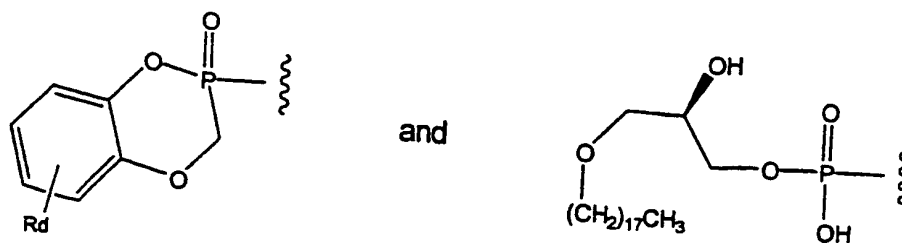


11. A compound of claim 2, wherein  $R^7$  is selected from the group consisting of:



15

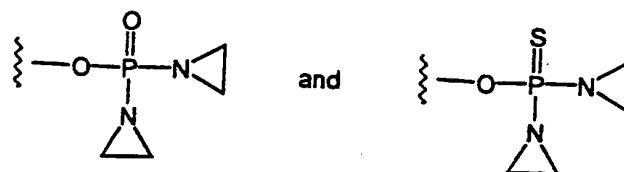
or a compound having the structure:



wherein  $R_d$  is an aromatic substituent.

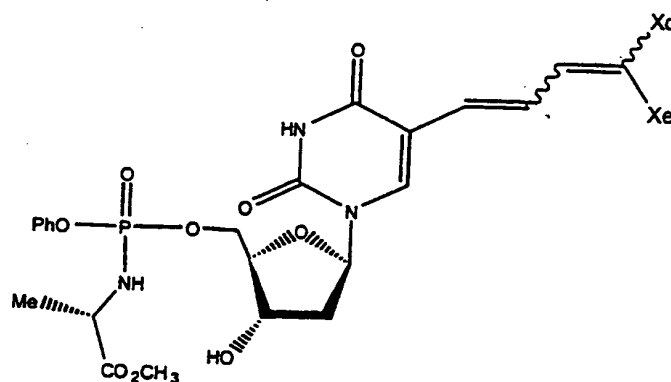
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12. A compound of claim 1, wherein  $R^4$  is selected from the group consisting of:



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13. A compound having the structure:

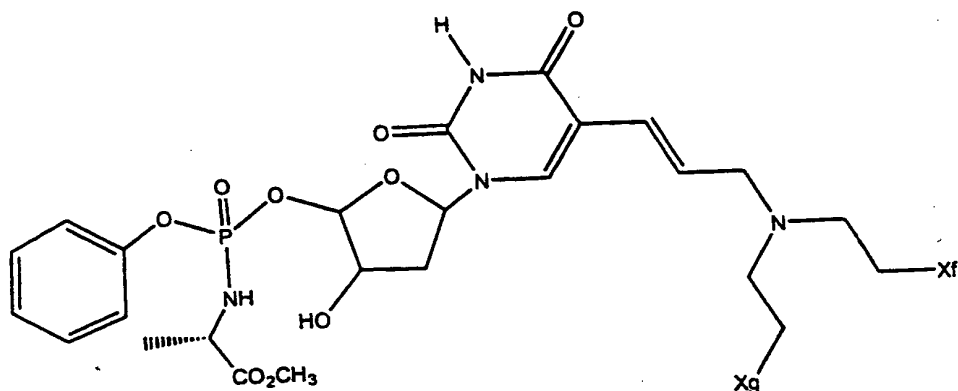


wherein  $X_d$  and  $X_e$  are independently the same or different and are selected from the group consisting of Cl, Br, I, and CN;  
or the nucleoside analogs thereof.

15

14. The compound of claim 13, wherein  $X_d$  is Cl or Br and  $X_e$  is H.

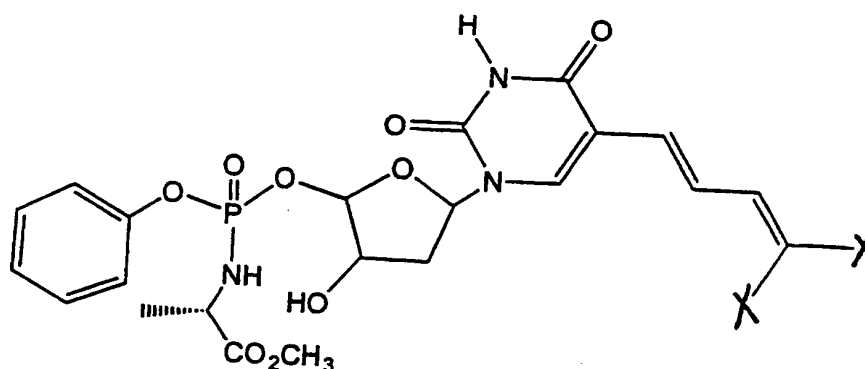
15. A compound having the structure:



5 wherein  $X_f$  and  $X_g$  are independently the same or different and are selected from  
the group consisting of Cl, Br, I, and CN;  
or the nucleoside analogs thereof.

16. The compound of claim 15, wherein  $X_f$  and  $X_g$  are the same and are each  
10 is Cl or Br.

17. A compound having the structure of the formula:

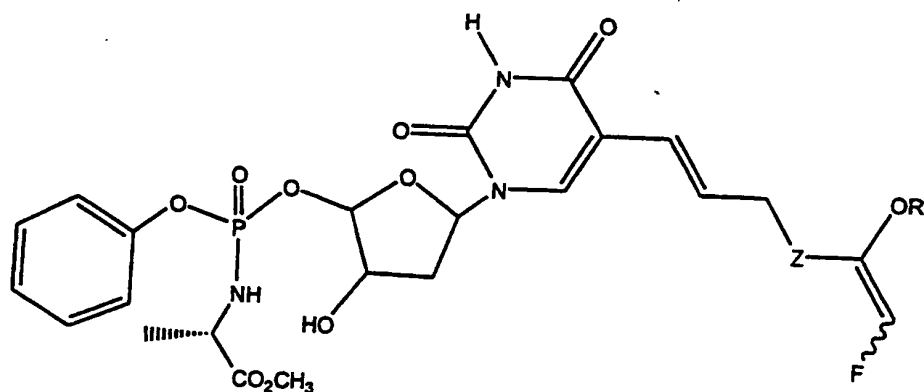


wherein each X is selected from the group consisting of Cl, Br, I, and CN;  
or the nucleoside analogs thereof.

18. The compound of claim 17, wherein X is Cl or Br.

19. The compound of claim 18, wherein X is Br.

20. A compound having the structure:

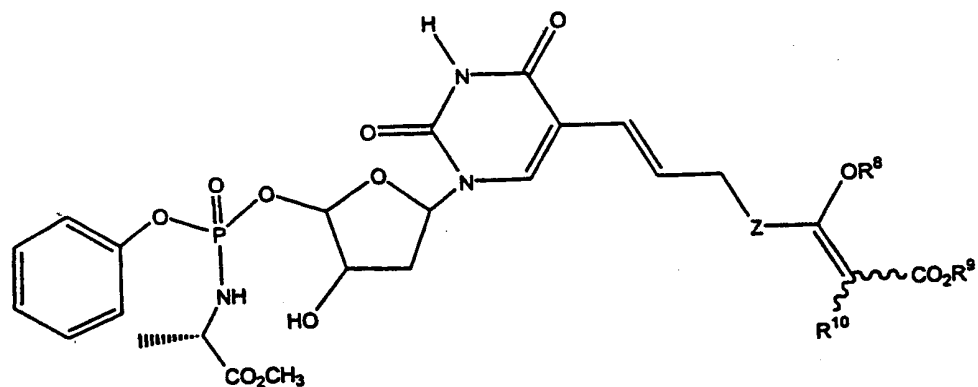




wherein  $R^8$  is a lower straight or branched chain alkyl;  
or the nucleoside analogs thereof.

5

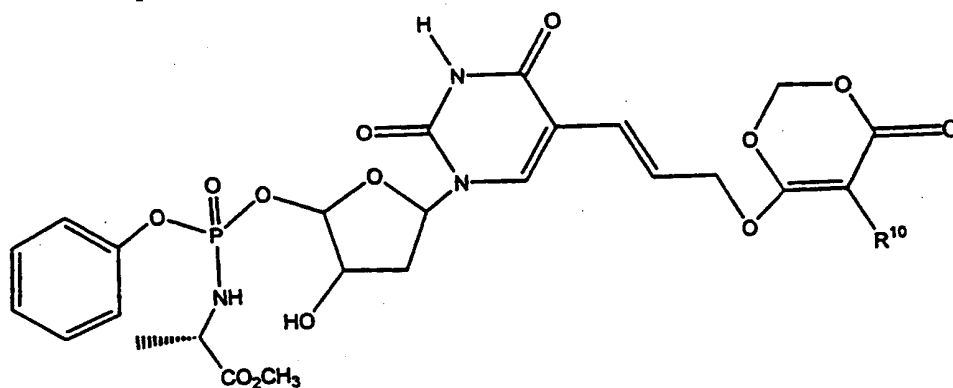
21. A compound having the structure:



wherein  $R^8$  and  $R^9$  are lower straight or branched chain alkyls and  $R^{10}$  is H or  
 $CH_3$ ;  
or the nucleoside analogs thereof.

10

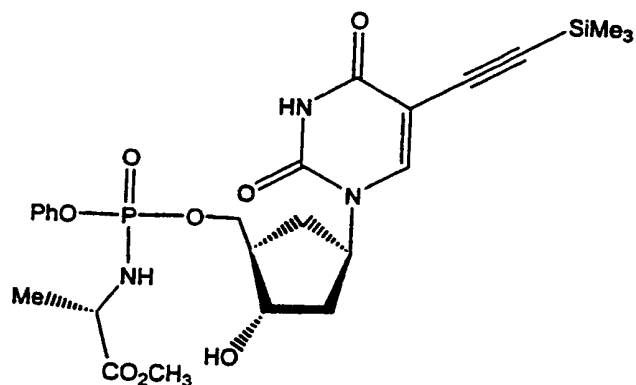
22. A compound having the structure:



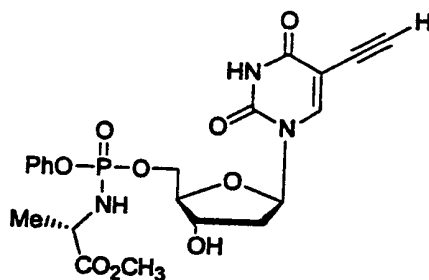
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wherein  $R^{10}$  is H or  $CH_3$ ; or the nucleoside analog thereof.

23. A compound having the structure:



24. A compound having the structure:

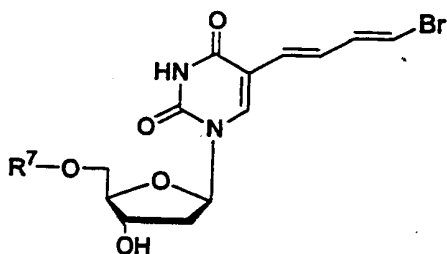


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or the nucleoside analog thereof.

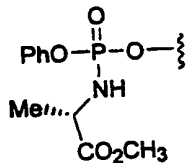
25. The compound of claim 1, wherein the compound has the structure:

10

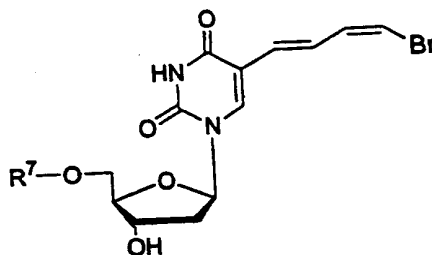


26. The compound of claim 25, wherein  $\text{R}^7 = \text{H}$ .

27. The compound of claim 25, wherein  $R^7$  is a substituent having the structure:

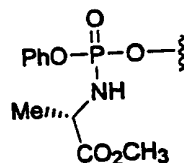


28. The compound of claim 1, wherein the compound has the structure:

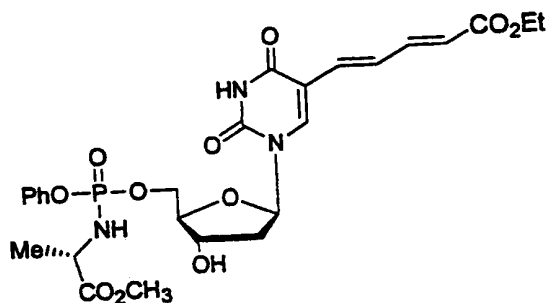


29. The compound of claim 28, wherein  $R^7 = H$ .

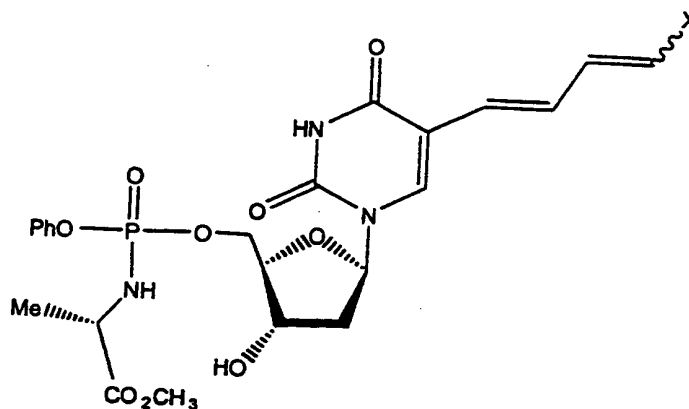
30. The compound of claim 28 wherein  $R^7$  is a substituent having the structure



31. A compound having the structure:

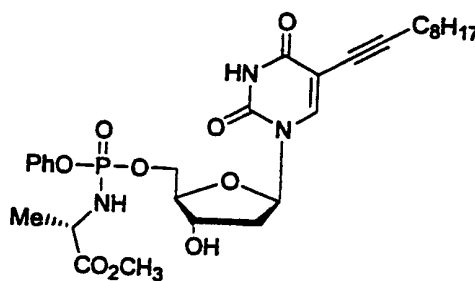


32. A compound having the structure:



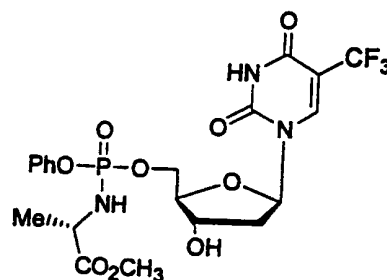
- wherein X is selected from the group consisting of  $\text{CO}_2\text{Et}$ , Cl, and Br,  
or the nucleoside analog thereof.

33. A compound having the structure:



or the nucleoside analog thereof.

34. A compound having the structure:



or the nucleoside analog thereof.

35. A composition comprising the compounds of claims 1 to 34, and a carrier.
36. The composition of claim 35, wherein the carrier is a pharmaceutically acceptable carrier.
37. A method for screening for a therapeutic agent, comprising:
- (a) contacting a sample containing a target cell with any of the compounds of claims 13 to 34;
  - (b) contacting a separate sample of the target cell with a potential therapeutic agent; and
  - (c) comparing the samples for inhibition of cellular proliferation or cell killing.
38. The method of claim 37, wherein the target cell is characterized as resistant to a chemotherapeutic drug.
39. The method of claim 37, wherein the target cell is characterized as expressing a target enzyme that is amplified as a result of selection *in vivo* by chemotherapy.
40. The method of claim 37, wherein the target enzyme is an endogenous intracellular enzyme that is overexpressed in the target cell.
41. Use of any of the compounds of claims 13 to 34 for the preparation of a medicament to treat or inhibit the proliferation of a pathological cell.
42. A method for inhibiting the proliferation of a pathological cell, comprising contacting the cell with an effective amount of any of the compounds of claims 13 to 34.
43. The method of claim 42, wherein the pathological cell is resistant to a chemotherapeutic drug.

44. The method of claim 42, wherein the pathological cell expresses a target enzyme that is amplified as a result of selection *in vivo* by chemotherapy.
- 5 45. The method of claim 44, wherein the target enzyme is an endogenous intracellular enzyme that is overexpressed in the target cell.
46. The method of claim 45, wherein the enzyme is thymidylate synthase.
- 10 47. A method for treating a pathology characterized by the proliferation of target cells in a subject comprising administering to the subject any of the compounds of claims 13 to 44.
- 15 48. The method of claim 47, wherein the target cell is resistant to a chemotherapeutic drug.
49. The method of claim 47, wherein the target cell expresses an enzyme that is amplified as a result of selection *in vivo* by chemotherapy.
- 20 50. The method of claim 49, wherein the target enzyme is an endogenous intracellular enzyme that is overexpressed in the target cell.
51. The method of claim 50, wherein the enzyme is thymidylate synthase.
- 25 52. The method of claim 48, further comprising contacting the cell with the prior chemotherapy after resistance to the prior chemotherapy has been reversed.